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- EXTERNAL REVIEW OF THE
ONCHOCERCIASIS CONTROL PROGRAM

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EXTERNAL REVIEW

OF THE

ONCHOCERCIASIS CONTROL PROGRAM

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ABBREVIATIONS

USAID	United States Agency for International Development
ATP	Annual Transmission Potential
AVV	Volta Valleys Development Agency
CMFL	Community Microfilarial Load
CSA	Committee of Sponsoring Agencies
EAC	Expert Advisory Committee
EG	Ecological Group
FAO	Food and Agriculture Organization of the United Nations
IBRD	International Bank for Reconstruction and Development
Mf	Microfilariae
NOC	National Onchocerciasis Committee
OCCGE	Organization for Coordination and Cooperation in the Campaign Against Endemic Diseases
OCP	Onchocerciasis Control Program
OCT	Onchocerciasis Chemotherapy Project
OFA	Onchocerciasis Fund Agreement
ORSTOM	Office for Scientific and Technical Research Overseas
PAG	Preparatory Assistance to Governments Mission
PDDT	Preclinical Drug Development Team
TDR	UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases
UNDP	United Nations Development Program
WHO	World Health Organization
WHO/AFRO	Africa Region Office of the World Health Organization

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PREFACE

The objectives and terms of reference (Annex 1) of the External Review cover a broad range of issues but focus, in particular, on progress made towards devolution. This report assesses OCP's achievements and institutional arrangements and highlights relevant issues; looking to the future and devolution, we have identified specific technical inputs and institutional arrangements that should help ensure that the Program eventually reaches a successful conclusion. We have also examined the work of the Onchocerciasis Chemotherapy Project (OCT) and issues concerning the socioeconomic development of the onchocerciasis areas.

The External Review team met with the Committee of Sponsoring Agencies (CSA) in Washington, D.C., prior to making field visits to the OCP Program area, and had the benefit of an early briefing by the Program Director, Dr. E. M. Samba. Field visits were carried out between May 2 and June 23, 1990. All eleven Participating Countries were visited by one or more members of the team.

Upon arrival in Ouagadougou, the team was fully briefed at OCP Headquarters before undertaking field visits. The briefing covered all aspects of OCP operations including administration, vector control, epidemiology, data analysis and computer support. Further briefings and discussions were held with OCP operational units at headquarters and with OCP personnel in Bamako (Mali), Kara (Togo), Odienne and Bouake (Ivory Coast), Hohoe (Ghana), Niamey (Niger), and with national personnel involved in OCP operations in Guinea, Guinea-Bissau and Sierra Leone. The frank and informative discussions held in the field were of great value to our understanding of the achievements and problems of the Program.

While in the Participating Countries, the team discussed the Program with ministers of health and members of the National Onchocerciasis Committees, wherever possible. Members of the team also met with country representatives of the World Bank, the United Nations Development Program (UNDP), the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). In the field, the team interviewed nationals employed by OCP and Program beneficiaries in local villages. The opportunity to attend the National Onchocerciasis Committees meeting and the Expert Advisory Committee meeting provided important insights into the working of these committees and their decision making processes. Members of the team also attended the first meeting of a task force on accelerated ivermectin distribution for the northern part of the Western Extension. The team leader also attended a Steering Committee meeting of the Onchocerciasis Chemotherapy Project in Geneva and met with members of the Preclinical Drug Development Team (PDDT).

Members of the team interviewed representatives of the sponsoring agencies and of several donor countries including Belgium, Canada, France, the United Kingdom, the Netherlands, Switzerland and the United States. Prior to completion of the report, the External Review team held a final meeting in Washington, D.C. from August 27 to August 31, 1990 and met with the CSA to discuss preliminary findings.

EXECUTIVE SUMMARY

The Onchocerciasis Control Programme has virtually eliminated transmission in the core area of the Program overcoming the major obstacles of resistance and reinvasion. It has made significant achievements in improving larviciding technology, in ecological monitoring to minimize environmental impact, in entomological research on the vector species, in epidemiological surveillance and assessment and in treatment of the disease. Protection of the OCP's achievements will require the continued commitment of the donors to the Program strategy based on vector control for a minimum of 14 years from the start of larviciding in any given area. The critical areas are the sources of reinvasion in the Western Extension and selected pockets in the core and Southern Extension areas. Maintaining the continued success of the Program will require continued support for the effective institutional arrangements that have allowed the Program to successfully pursue its mandate with autonomy and flexibility within a framework of internal checks and balances through independent expert review and oversight from the sponsoring agencies, donors, and Participating Countries.

The success of the Program can be attributed to: clearly defined objectives; a realistic timeframe; choice of the best technology available for the tasks at hand; the high susceptibility of onchocerciasis to vector control due to the breeding habits of the vector; contracting out of highly specialized tasks; the priority given to operational research; the high degree of autonomy of the Program; the delegation of authority within the governing structure which has permitted timely response to changing requirements in the field; long-term commitment from donors, sponsors and Participating Countries within six-year financial planning cycles which have specified medium-term operational goals; an effective system of checks and balances characterized by transparency and free flow of information between the Program, its statutory review bodies, and the governing structure - the CSA and the Joint Programme Committee (JPC); and finally, strong vertical management and high quality staff.

The Program and its sponsors, donors and Participating Countries must now turn their full attention to devolution. The future of the Program is clearer today given the availability of an effective microfilaricide, ivermectin. However, the institutional dimensions and the financing mechanisms to assure successful devolution need to be spelled out and made operational, as the Program enters its fourth financial phase. The technological underpinnings for devolution will be epidemiological surveillance and ivermectin distribution for disease treatment and recrudescence control. The effective implementation of these activities will require appropriate institutional strengthening in the Participating Countries with special attention to training and management.

OCP can contribute further to devolution through creation of a new Devolution Unit, with three or four professionals (a social scientist, epidemiologist, public health/management specialist, and training specialist), which would: (i) design and undertake training and in-service training in management, multi-disease surveillance, and drug distribution; (ii) promote greater involvement of national team personnel in strategic planning,

supervision, and evaluation; (iii) contract new personnel specialized in public health and institutional development to maximize the OCP contribution to general health systems development; (iv) sensitize Participating Country governments to the importance of onchocerciasis control maintenance as a national priority and to the need to absorb the highly qualified personnel trained by OCP; (v) sensitize Participating Countries to the increasing importance of community education and mobilization efforts as disease control efforts rely increasingly on epidemiological surveillance and ivermectin treatment; (vii) support operational research on topics relevant to devolution; (viii) provide technical assistance to Participating Country governments to strengthen the organization and management of disease control.

In regard to devolution, there are a number of research topics that should be pursued: the impact of ivermectin on transmission in real recrudescence situations; the relative effectiveness of alternative ivermectin distribution systems; the safety of ivermectin on more frequent dosage schedules; potential resistance to ivermectin and appropriate tools to detect such resistance; general health systems research in the Participating Countries; and development of a highly sensitive and specific immunodiagnostic test to detect low levels of infection.

The Onchocerciasis Chemotherapy Project (OCT) has been of great value. The field trials for ivermectin were instrumental in preparing for selective mass treatment of onchocerciasis. Its primary objective, however, is to search for a safe and effective macrofilaricide and an increased number of compounds from as many pharmaceutical sources as possible should be screened. The new OCP/TDR Macrofil Project, combining the efforts of OCT and the Special Programme for Research and Training in Tropical Diseases (TDR) is a positive step but must not be allowed to dilute the OCT objective nor to reduce its flexibility, within the bureaucratic framework of TDR.

In the longer term, an intercountry facility will be needed to provide a framework for intercountry cooperation and for activities which are beyond the capacity of the Participating Countries. Such a facility would: monitor epidemiological trends throughout the Program area; coordinate the efforts of regional institutes involved in onchocerciasis research; assist in data processing and provide a long-term memory for analysis of trends; help countries determine needs and priorities; undertake training, review research and disseminate information.

Participating Country capacity for development of the onchocerciasis areas is very limited and separate planning for these areas, outside the national economic context, is inefficient. We recommend that the CSA, interested donors and Participating Countries jointly support a review of what the CSA socioeconomic development program has produced and what it means for each of the Participating Countries. This review should be carried out by a team of economists and social scientists, working closely with Participating Country officials. Its primary objective should be to summarize and examine these conclusions in the specific socioeconomic development context of each of the Participating Countries. Such a review should help strengthen socioeconomic development planning with respect to the onchocerciasis areas and ensure the integration of such planning into the broader national development strategy of each of the Participating Countries.

I. ACHIEVEMENTS OF THE PROGRAM

A. Progress in OCP Operations

1. Few programs can claim the kind of success that the OCP, in spite of serious obstacles, has achieved in the past 16 years. In all of the original Program area the disease has ceased to be a public health problem. Today, over 30 million people (including the populations of both the Western and Southern extension areas) are protected from the transmission of onchocerciasis and its symptoms because of the OCP. Since the Program began, about seven million children have been born virtually free of risk of onchocercal blindness. Some 1.25 million people who were at one time seriously infected are today completely free of the parasite. Furthermore, there are about 100,000 people in the Program area who still have their sight today because of the OCP. The OCP is also having significant net socioeconomic benefits which can be quantified (Benton and Skinner 1990). The Program's accomplishments have been many, in particular, it has made advances in: (i) vector control and larviciding; (ii) ecological monitoring (iii) entomological research; (iv) epidemiological assessment; and (v) disease treatment.

Vector Control

2. OCP vector control operations have been highly successful, in spite of the great difficulties posed by resistance to larvicides and reinvasion of controlled areas. These were no small obstacles, but with the backing of a committed donor community, strong program management and operational flexibility based on applied research, the goals of the Program were not compromised. A highly effective radio network maintained by the Program throughout the Program area has been fundamental to the efficient management of vector control; this communications system should be useful to the Participating Countries (and to an intercountry facility) for onchocerciasis and other disease control efforts for many years to come. Today, with the exception of some pockets of resistance or reinvasion, the following indicators apply throughout the original Program area: (i) annual biting rate is below 100 and annual transmission potential is less than ten (these measures indicate that there is no significant risk of onchocerciasis transmission); (ii) community microfilarial load (CMFL - the mean number of microfilariae per skin snip for a given population) has reached a very low level (between 1 and 4); (iv) prevalence of blindness due to onchocerciasis is clearly in decline; and (v) prevalence of onchocerciasis is in marked decline. Thus, there are grounds for optimism and the original area is in an excellent position to begin devolution.

3. The vector control strategy should be able to achieve similar results in the extension areas, eliminating the sources of reinvasion of the original area. In the Southern Extension area, vector control is now in its 3rd year and has had good results with the exception of two problem areas located on the Benin/Nigeria and Ghana/Togo borders. Vector control operations are now

underway throughout the Western Extension with the exception of the northern part (western Mali, Senegal, and Guinea Bissau) where larviciding operations have been discontinued.

Larviciding

4. The OCP's rotational larvicide use has successfully prevented any serious interruption of operations due to blackfly resistance to larvicides and the search for new compounds (especially from groups unlikely to give cross-resistance) has been diligently pursued. In addition, the Program has improved larviciding operations in two respects: (i) it has improved accuracy in larvicide application and consequently, cost-effectiveness; and (ii) it has improved its capacity to judge when spraying may be safely discontinued.

5. The OCP has upgraded larviciding operations with the introduction of a computer program (PERLES), developed by ORSTOM hydrologists in 1989. This program optimizes larvicide and application costs by embracing simultaneously all relevant larvicide, river (discharge) and aircraft parameters.[1] Using this technology, the Program has realized considerable savings in larvicide and application costs.

6. For the original area, OCP's attention is focused largely on defining the parameters on which the decision to stop larviciding can be based. Epidemiological mapping and entomological surveillance activities are being complemented by another computer model, ONCHOSIM, which predicts long-term epidemiological trends given control methods based on specific combinations of vector control and ivermectin treatment. The Program's technical staff hold that larviciding can be stopped after 14 years if the following criteria are met: (i) trends in CMFL and trends in prevalence of cohorts in the indicator villages should be the same as or faster than the trends predicted assuming complete interruption of transmission; (ii) in indicator villages, there should be no incidence in children born since the beginning of vector control or in persons skin snipped twice with negative results on both occasions. For non-indicator villages, prevalence and distribution of microfilariae (mf) should be consistent with that found in the indicator villages[2].

Ecological Monitoring

7. The Program, guided by the independent advice of the Ecological Group, has continually conducted tests to determine the impact of new larvicides and new formulations on the environment and has evaluated the long-term impact of

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[1] The program is based on "Graph and Network" mathematical theory and on OCP's prediction models for the carry of larvicides in water-courses under all conditions occurring in the program area. These models were developed for larvicides in use on the basis of experimental river applications, use of fluorescent tracer, and bioassays.

[2] OCP will continue entomological surveillance and evaluation for two years after larviciding stops in order to determine the proportion of infective parous flies (OCP 1990a).

vector control operations on the non-target fauna. Thus far, no long-term effect on the fauna has been revealed by analyses of available data. OCP is currently working on development of a technique by which long term effects can be determined by short term observations and steps have been taken to improve the processing, analysis and presentation of hydrobiological data (Yameogo et al. 1988; OCP 1990b).

Entomological Research

8. The OCP has made considerable improvements in its ability to detect resistance to larvicides. Thresholds of resistance for S. damnosum s.l. populations have been reassessed and a computerized cytotaxonomic data bank has been developed. The cytotaxonomic data can thus be correlated with known resistance patterns. This facilitates redefinition of the range of susceptibility of the various members of the S.damnosum complex.

9. Operational research on the vector continues to improve OCP's ability to target vector control. OCP continues to seek a better understanding of the distribution of vector species and to add to its knowledge of their respective roles in transmission. Studies of vector species distribution have been concentrated in southern Sierra Leone and nine species or forms have now been identified. Pending the separation of infective larvae recovered from man-biting vectors into blinding and non-blinding strains, the decisions on which vectors should be targeted for control will depend on "cross-transmission studies and knowledge of man-biting rates, anthropophily, survival rates, natural infection levels and associations with blinding foci' (OCP 1990a).

Epidemiological Assessment

10. OCP studies of the epidemiological impact of ivermectin treatment have established that ivermectin probably cannot effectively control onchocerciasis transmission on an annual treatment schedule (in hyper and holo-endemic areas). More research is underway to assess its epidemiological impact at more frequent dosage schedules (e.g. several years of treatments at 3 to 4 month intervals). OCP also recognizes that it may not be possible to measure the impact on transmission until after 7 to 8 years of ivermectin treatments (OCP 1990a; OCP 1990c).

11. OCP has completed epidemiological mapping throughout the original and extension areas. These surveys are essential to strategic planning, including the selection of communities for chemotherapy delivery.

12. The OCP's epidemiological surveys show that priority areas in the Western Extension area (areas of high endemicity and high risk of blindness), are situated in the Upper Niger Basin, the Gambia Basin in Senegal, Upper Bakoye Basin, and the Tienfala focus along the Niger River in Mali.

13. In addition, studies of ocular disease patterns (through ophthalmological examinations) in selected villages in the Upper Niger basin in Guinea and Sierra Leone have led to a better understanding of the relationship between the prevalence of severe eye lesions, onchocercal

blindness, and CMFL.[3] These findings have helped OCP to better target vector control by determining the southern limit of the transmission of blinding forms of the parasite and, therefore, the southern limit for vector control and targeted ivermectin delivery.[4]

14. The ONCHOSIM computer model, mentioned above, also permits the separate simulation of lesions of the anterior and posterior segments of the eye. It may, therefore, facilitate more realistic simulation of morbidity control following treatment with ivermectin. Two important sensitivity analyses were carried out by the University of Rotterdam, which has been collaborating with the OCP on epidemiological research. The first of these concerned a detailed analysis of the parameters which control the distribution of the lifespan of O. volvulus. The main conclusion was that the mean reproductive lifespan of O. volvulus is between 9 and 11 years and that 95% of the adult worms terminate their reproductive period before the worm age of 13 to 14 years. The second sensitivity analysis addressed the risk of recrudescence in relation to duration of vector control. The results confirmed previous estimates that the risk of recrudescence continued to be too great after 13 years of control, and that a minimum of 14 years of interrupted transmission is required. Further refinements with combinations of different parameter quantifications indicated that some risk of transmission existed even after 14 years. Further modelling considerations related to data analysis and operational planning have been made, including: quantification and testing of the ocular disease module; simulation of regional variations in transmission dynamics; and surveillance and recrudescence control under devolution (OCP 1989; Remme et al. 1986).

15. It may soon be easier to distinguish blinding from non-blinding strains of the parasite if a DNA probe, currently under study by the OCP and the University of Alabama, is validated. It may also be of value in distinguishing human and animal strains of the parasite.

Disease Treatment

16. Clinical trials conducted by the OCP (Tamale/Hohoe) have established that ivermectin has a profound microfilaricidal action, reducing mf loads for up to one year. The safety of ivermectin (following individual treatments)

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[3] The community patterns of ocular onchocerciasis in these areas were compared with patterns found in the savanna zone of the original area. The result was that at similar levels of CMFL, the corneal microfilarial load in the community and the prevalence of advanced sclerosing keratitis proved to be much lower in Guinea and Sierra Leone. In northern Sierra Leone, patterns of infection suggested the presence of another non-blinding strain and further ophthalmological investigations are being undertaken by the OCP.

[4] In Sierra Leone there was a linear relationship between CMFL and severity of eye lesions. Although incidence of blindness was lower than in the original OCP area, onchocercal blindness reached significant levels (4 to 6%) where CMFL levels were high.

has been established in clinical trials and through observations made in the execution of targeted ivermectin treatment.

17. The potential role of ivermectin in the prevention of disease may be much greater than earlier believed. Annual treatment with ivermectin has been shown (in the savanna area) to cause regression of iridocyclitis and sclerosing keratitis, and to arrest optic atrophy and choroidoretinitis. The positive clinical results of ivermectin treatment suggest that exclusion criteria should be revised to make the drug available to more heavily infected patients (OCP 1990a; Remme et al. 1989; Dadzie et al. 1986, 1989).

B. Reasons for Success and Lessons Learned

18. There are many interdependent characteristics of the OCP which are clearly factors that have allowed the Program to achieve what has been achieved to date -- the near eradication of a serious public health problem from a large and often inaccessible area. The success of the Program can be attributed to: (i) clearly defined objectives; (ii) a realistic and feasible time frame; (iii) choice of the right technology; (iv) the susceptibility of onchocerciasis transmission to control; (v) contracting out of highly specialized operations; (vi) a strong emphasis on operational research; (vii) a high degree of autonomy from WHO and its governing structures; (viii) clear delegation of authority allowing operational flexibility; (ix) medium-term planning and sustained donor commitment; (x) an unrestricted flow of information between all parties concerned which has helped to maintain a system of internal checks and balances and clear accountability; and (xi) strong management and high quality staff.

Clearly Defined Objectives

19. Since its inception the OCP has held to a limited, well-defined objective that has been shared equally by Program staff, beneficiaries, donors and sponsoring agencies. This has given the Program a clear mandate and the legitimacy to pursue it. Consequently, the Program's highly focused nature helped ensure that it was guided by rigorously technical, not political, considerations. Such single-mindedness of purpose has been a critical dimension in the successful implementation and day-to-day management of the Program.

Realistic Timeframe

20. The OCP and the donors agreed at the beginning of the Program on a realistic timeframe for achievement of Program objectives. The request for a 20-year commitment from the donors was unprecedented and did not meet with immediate approval from the potential donors. Nonetheless, the proponents of the Program remained firm in their assessment that this timeframe was appropriate and realistic based on epidemiological facts (principally the then conceived 15 to 18 year lifespan of the adult worm).

Choice of Technology

21. Part of the Program's success can be attributed to its conscientious pursuit of the best technology available. This has allowed a sophisticated level of operational control hardly imagined possible in West Africa. Accordingly, aircraft have been used to apply larvicides and, more recently, water level data have been transmitted using state of the art methods via satellite enabling more accurate spraying levels and reduced environmental impact. Computer modelling of onchocerciasis transmission has been developed and is used in forecasting the progress of operations. Chromosome reading was introduced to identify species of the S. dammosum complex more efficiently and the separation of vector and non-vector species. This reliance on the most advanced tools available has helped maintain the cost-efficiency of operations.

Susceptibility of Onchocerciasis Transmission to Control

22. In part, the Program's success must be attributed to the nature of onchocerciasis transmission. The disease proved highly susceptible to the control strategy applied because it was possible to pinpoint very precisely the locations of vector breeding sites, the characteristics of vector migrations, and the pattern of fluctuations in the hydrographic network. Other vector-borne disease control efforts (malaria, for example) have not shared this kind of advantage.

Contracting Out Highly Specialized Tasks

23. Aerial spraying operations, the key element in the OCP strategy, were contracted out to private companies especially qualified for the task. The OCP accepted early on that it lacked the expertise to undertake such a large and complex spraying effort involving a fleet of helicopters and sophisticated spraying equipment.

Operational Research

24. Much of the Program's success can be attributed to the importance granted to operational research. Since the Program began from a position of relative ignorance and inexperience, operational research was a key element in the development and evolution of the OCP's disease control strategy. OCP has spent about 15% of its budget on operational research. Results of operational research have guided operations and helped improve efficiency. Operational research has focused on a range of relevant problems such as: larvicide development and application technologies, vectorial capacity and vector species identification, the relationship between intensity of infection and blindness, the epidemiological impact of control efforts, and clinical ivermectin field trials.

Autonomy of the Program

25. The Program was set up with a high degree of autonomy. Specifically, it has never come under the direct jurisdiction of the World Health Assembly or the WHO Executive Board. This has helped OCP avoid WHO bureaucratic

procedures, enabling it to adjust operations quickly when necessary. OCP's autonomy has sheltered the Program from competition with other WHO priorities during a time when attention to tropical diseases has clearly declined.

Governance of the Program

26. Delegation of authority to those most closely involved in the Program has been crucial to assuring its ongoing success. The Committee of Sponsoring Agencies (CSA), which meets three to four times per year, has proven a useful, persistent referee of the OCP since the beginning. The delegation of responsibility for policy development and financial supervision to the CSA has enabled crucial decisions to be taken between annual meetings of the JPC. This has allowed the Program to respond in timely fashion to changing operational and financial requirements.

Medium-Term Planning and Sustained Donor Commitment

27. Faced with the difficulty of sustaining donor support over a long period, the Program was divided into a series of six-year phases. A detailed plan of operations was prepared for each phase outlining the objectives to be reached during that period, any modifications necessary and the estimated cost of the operations. The Onchocerciasis Fund Agreements, based on approved Plans of Operations, bind the Program to what it should accomplish in the six-year period, obligate the donors to an agreed upon level of financial support, and tie the Participating Countries to their responsibilities.

Transparency - Information Flow

28. The Program has benefited greatly from the transparency achieved by maintaining an unrestricted flow of information about the Program amongst all parties involved. It has also benefitted from its own openness to inspection and review. The Program has undergone annual technical audits by the EAC which has reported its findings in frank annual reports to the JPC. Periodic analyses and reviews by the EAC and the Ecological Group have strengthened the Program by providing independent, credible evaluation of activities and progress. They have also endorsed necessary modifications in strategy or tactics. The oversight provided by these statutory bodies have enabled the JPC to maintain donor confidence and support. Another important input has come from independent reviews including the Independent Commission Report in 1981 (WHO 1981), the USAID Impact Review in 1985 (USAID 1986) and the present External Review.

Strong Management and High Quality Staff

29. OCP management of human, material and financial resources is rigorous and strict and almost military in character. This yields a certain optimism with respect to the achievement of Program goals, a sense of urgency to act and to succeed, and an overriding sense of the importance of discipline and order. There is also a sense of honor and pride in one's work and in the mandate of the Program as a whole. Out of this develops a sense of family and team spirit. Discipline is high and OCP personnel take their jobs very

seriously; each staff member is aware of how important his particular task is to the success of the Program.

Lessons Learned

30. Goals must be set within a realistic timeframe. A key factor in sustaining donor commitment over the long term was the acceptance, at the very beginning of the Program, of a long-term perspective and commitment, which was based on epidemiological fact (the lifespan of the adult worm).

31. Maintaining this level of commitment over time requires that goals be clear and unambiguous and that progress towards them be updated frequently and assessed regularly by independent reviews.

32. The legal nature of the formal Onchocerciasis Trust Fund Agreements (covering six-year periods) has also been very important in maintaining donor commitment and in maintaining the organizational integrity of the Program. In addition, the division of the corresponding six-year financial phases into annual budget cycles has enhanced transparency and accountability and further maintained the confidence of the donors.

33. Operational research is essential. It can increase efficiency and reduce costs, and ensure survival of a program when critical technical challenges arise (the rapid spread of resistance to larvicides, for example).

34. Under certain circumstances, technologically advanced alternatives can be more cost-effective than others. In the Program's experience, the highly sophisticated aerial larviciding operations have proven to be a great deal less costly, and certainly more effective, than ground larviciding would have been.

35. The Program has been able to maintain better control and demand higher quality in vector control operations by contracting out aerial larviciding to competent, specialized firms. Better results can be achieved more efficiently when highly specialized tasks, beyond the expertise of the executing agency, are contracted out in this way.

36. The Program's autonomy from WHO and its governing bodies helped insulate the Program from competition with other health development trends in Africa and a useful lesson can be drawn from the fact that the Program has prospered at a time when attention to tropical diseases, in general, has been in serious decline.

II. DEVOLUTION

A. Background

37. The idea that the Participating Countries would eventually assume full responsibility for maintenance of onchocerciasis control was first discussed in the PAG mission report in 1973 (UNDP/FAO/IBRD/WHO 1973). The concept of "devolution", or the process by which responsibility for onchocerciasis control would be transferred to the Participating Countries, was first articulated as such by the Independent Commission in 1981 (WHO 1981). The Long Term Strategy paper (OCP 1984) went further to define devolution as a long term objective of the Program which would be carried out jointly by the Program and the Participating Countries. Translating the concept into action, however, proved difficult due to the Program's reliance on highly sophisticated technology and on strong, vertical management. Technological and institutional constraints have made it impossible to transfer much of what OCP does to any one of the Participating Countries. However, with the introduction of ivermectin, devolution and its objectives could be more clearly defined in operational terms. Devolution is now understood to mean progressive national participation in activities to detect and suppress recrudescence and in the distribution of ivermectin to reduce morbidity (OCP 1988:1). Thus far, devolution plans have been approved by the JPC for Mali, Niger, and Burkina Faso (see Annex 2) and draft plans are soon to be submitted for Benin, Ghana, Ivory Coast, and Togo.

38. Presently, the Programme's contribution to devolution includes: (i) the development of technical standards and evaluation of entomological and epidemiological surveillance; (ii) advisory and coordination activities regarding the development of national plans for devolution, including efforts for attracting external financing; and (iii) training of nationals in fields relating to OCP operations. The OCP draft Plan of Operations for 1992-1997 adds training and research in new fields relating to health care systems and management to these activities.

39. The Participating Countries already take part in epidemiological evaluation and ivermectin distribution under OCP supervision. They also possess the capability to carry out ground larviciding and entomological surveillance. In addition, with technical assistance they could assume full responsibility for ecological monitoring. The specific OCP activities which cannot be devolved (and which would have to be passed on to a successor agency to OCP) are aerial larviciding, new larvicide development, and macrofilaricide research. The Participating Countries do not have and are unlikely to achieve, in the foreseeable future, the technological, institutional, or financial capacity to take on these specific activities.

B. Requirements for Maintaining Onchocerciasis Control

In order to maintain onchocerciasis control, the Participating Countries must have the capacity to: (i) detect recrudescence through epidemiological surveillance; (ii) suppress recrudescence (i.e. renewed transmission) in very

limited foci using ivermectin; and (iii) carry out ivermectin treatment to reduce morbidity (i.e. for disease control).

Detecting Recrudescence

40. The existing system to detect recrudescence consists of: (i) passive screening at public and private health centers in order to detect infected cases among patients presenting spontaneously; (ii) if high levels of infection were detected, skin-snip surveys would be carried out by mobile teams in areas of suspected recrudescence (migration studies would complement this system); and (iii) monitoring levels of infection through skin-snip surveys in randomly selected indicator villages every three years. Nationals are already involved in this surveillance system, under the close supervision and with the logistic and financial support of the OCP. Under devolution, these activities will become the full responsibility of the Participating Countries.[1]

Suppressing Recrudescence with Ivermectin

41. There are still some major questions about this particular aspect of devolution and maintenance of onchocerciasis control which cannot be answered today and which will require, at least, several years of observations of the epidemiological impact of ivermectin use[2]. The EAC has summarized the question of ivermectin and recrudescence (transmission) control thus: "the OCP still needs to determine the degree to which ivermectin can control transmission in a true recrudescence focus, what critical threshold should be reached before ivermectin delivery should be undertaken, and the best dosage frequency to achieve control. Such a focus has yet to be found in the OCP area" (OCP 1990a:6). The available evidence suggests that ivermectin does not have a significant impact on transmission when given on a yearly dosage schedule and under present exclusion criteria (which so far has permitted coverage of about 60-65%). In order to assess its usefulness as a

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[1]In areas at risk where vector control is not carried out (such as the northern part of the Western Extension area) surveillance activities would not aim to detect recrudescence but would focus on detecting persons at risk of blindness or serious skin disease using clinical methods. This could be done by screening for corneal lesions with a magnifying glass which, according to ophthalmologists, would be possible for health workers with limited training. The skin-snip method could still be used to determine severity of infection in individuals.

[2]Computer simulations using the ONCHOSIM epidemiological model quantified the effect of ivermectin, based on results from the community trial in Asubende, and concluded that large scale ivermectin treatment alone cannot progressively eliminate the parasite resevoir in endemic areas in West African savanna. This was supported by the latest field observations from the Asubende focus. There are still uncertainties about long term impact of ivermectin treatment, mf repopulation dynamics after treatment, and the cumulative effect of repeated treatment on mf production.

transmission control tool, there is a need for an evaluation of the results on transmission of several years of ivermectin treatments at 3 to 4 month intervals. Although the OCP lacks experience in the use of ivermectin to suppress recrudescence, it will hopefully collect relevant information on the epidemiological impact of ivermectin in the northern part of the Western Extension where vector control is being discontinued and ivermectin distribution intensified. A review of the epidemiological impact of ivermectin, as well as of drug delivery systems and of the safety of repeated treatments at more frequent intervals, should be made in 5 to 6 years, if possible, to reassess its role in transmission and disease control strategy.[3]

42. In any event, the Participating Countries will have to be prepared to respond to recrudescence situations with the tools available, i.e. through either targetted ivermectin delivery or, where feasible, limited ground larviciding. In spite of the uncertainties regarding ivermectin and suppression of recrudescence, Participating Country capability to undertake these activities must be strengthened in the course of devolution.

Ivermectin Distribution to Control Disease

43. The prospect for control of disease manifestations with ivermectin is very good[4]. About 35,000 people are being treated per year in all high risk areas (defined as areas where the community microfilarial load, CMFL, is found to be greater than 10 microfilariae per skin-snip). Selective ivermectin distribution for disease control is being carried out primarily in the extension areas where larviciding is still underway or where larviciding will not be carried out. Drug distribution is carried out by nationals under the direct supervision and with financial and logistic support of the OCP. This is expected to continue for as long as the OCP is in operation. In devolution

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[3] In the Western Extension area there are likely to be some difficulties in assessing epidemiological impact due to the presence of animal (onchocerciasis) larvae in the vectors throughout the area. Furthermore, a reduction in incidence would be difficult to determine during the initial 4 to 5 years of treatments due to the length of the pre-patent period (the period before the adult worms begin producing microfilariae), the low sensitivity of skin-snips to light infections, and the lack of a control group. It may, in fact, only be possible to clearly observe the epidemiological impact of ivermectin on transmission after 7 to 8 years of treatment (OCP 1990c).

[4] Observations in the savanna area showed that annual treatment with ivermectin caused regression of iridocyclitis and sclerosing keratitis, and arrest of optic atrophy and choroidoretinitis. Clinical results from two rounds of ivermectin treatment have shown improvement or stabilization of eye lesions. This suggests that the exclusion criteria should be reviewed to enable maximum availability of such benefits to more heavily infected patients and, in holo-endemic areas, annual treatment may be recommended (OCP 1990a; Remme et al 1989; Dadzie et al. 1989).

this activity will, in most of the Participating Countries, be horizontally integrated with other disease control activities. The Participating Countries must now begin to consider and experiment with alternative distribution mechanisms in order to optimize the potential benefits of the drug to affected populations.

Research to Define the Parameters of Ivermectin Use

44. There are a number of operational research tasks which would help answer some of the major questions related to successful maintenance of onchocerciasis control. We have already mentioned the need for studies of the impact of ivermectin on transmission at more frequent dosages (e.g. 3 to 4 month intervals). In addition, further research is needed to determine the incidence level at which recrudescence control using ivermectin must be initiated. The minimum safe interval between ivermectin treatments also needs to be established. It is possible that ivermectin may be less effective in early infections; if so, this needs to be better understood and its implications for detecting recrudescence considered. More needs to be known about the efficacy of ivermectin treatment over a prolonged period in preventing, halting or reversing eye disease. Since there is known resistance to ivermectin in veterinary medicine and since ivermectin will assume a greater role in onchocerciasis control (e.g. the northern part of the Western Extension) research on potential resistance to ivermectin should be pursued through the OCP/TDR Macrofil Project.

45. Research on alternative ivermectin delivery systems, within the specific context of each of the Participating Countrys' existing health systems, is especially important and should: (i) determine the actual logistic requirements for ivermectin delivery through active (seeking out infected individuals and treating them) and passive (making the drug available to patients seeking treatment) distribution mechanisms; (ii) provide an estimate of the actual need (i.e. the number of patients that will require treatment) (iii) examine different methods of organizing drug delivery (e.g. alternating distribution from fixed and mobile facilities, inventory management and storage systems, recordkeeping systems on individuals and communities, supervision/monitoring systems); (iv) examine simultaneous distribution, in the course of the same round, of various therapeutic agents; (v) attempt to determine the optimal length and frequency of rounds; (vi) examine behavioral issues concerning the acceptance and use of the drug, for example, will use of the drug for treating human intestinal parasites, or for treating bovine parasites affect its use for onchocerciasis? In the absence of reinfection, treatment must be repeated annually until all adult worms have died (an estimated 11 years); will patients comply throughout this extended period, however, in the probable absence of symptoms?.

46. The JPC should also seek increased support for ongoing research and development of an appropriate immunodiagnostic test which can better detect of low levels of infection. Several university laboratories are already involved in this research which is especially important in terms of the capability to detect recrudescence. If it is possible to suppress recrudescence through ivermectin treatment, then the OCP's epidemiological modelling studies suggest

that the sooner intervention begins the greater the chances of success (OCP 1989:7).

C. Institutional Aspects of Devolution

47. Devolution is essentially the process of strengthening Participating Country capabilities in epidemiological surveillance and ivermectin distribution, with the goals of detecting and suppressing recrudescence of onchocerciasis. The sustainability and impact of devolution can be better assured and amplified if it is carried out as part of general health systems development in the Participating Countries. OCP can meet the needs of devolution and contribute to health systems development by undertaking activities in two general areas where it already has considerable experience: (i) training and in-service training; and (ii) technical assistance, especially in regard to planning, management and operational research.

Creating an OCP Devolution Unit

48. The Program can begin by creating a Devolution Unit to undertake activities in these areas. Specifically the unit would:

(i) design and manage training and in-service training programs for field personnel involved in multi-disease surveillance and drug distribution activities -- each country requires a human resource development plan, based on an in depth assessment of existing human resources and projected needs (the OCP has already contracted two consultants to begin this work);

(ii) undertake a management training program for mid- and upper level national personnel with a focus on personnel management skills, instilling discipline and positive work attitudes

(iii) promote greater involvement of national team personnel, at all levels, in strategic planning, supervision, and evaluation.

(iv) contract new personnel specialized in public health and institutional development to maximize the OCP contribution to general health systems development (these professionals could begin by seeking new ways to enhance the productive interaction between OCP and national institutions);

(v) sensitize Participating Country governments to the importance of onchocerciasis control maintenance, promote its establishment as a high priority in public health, and make Participating Country governments aware of the human resources that are being trained by OCP and the need for Participating Countries to make appropriate plans for the eventual absorption of these highly qualified personnel.

(vi) sensitize Participating Countries to the increasing importance of community education and mobilization efforts as disease control efforts rely increasingly on epidemiological surveillance and ivermectin treatment. In each country, community mobilization plans are needed;

knowledge, attitude, and practice (KAP) surveys could usefully identify gaps in knowledge about onchocerciasis, attitudes towards the disease and in those who are afflicted, and the appropriate content and vehicles for disseminating public health messages.

(vii) support operational research on topics relevant to devolution such as health systems research (basically, inventories of what actually exists in the Participating Countries need to be updated); alternative ivermectin delivery systems; ivermectin's epidemiological impact and long term safety; new immunodiagnostic tools; drug resistance; and community participation in onchocerciasis control;

(vii) provide technical assistance to Participating Country governments to help them strengthen the organization and management of disease control in general;

49. The initial size and professional composition of such a unit should be determined by OCP management on the basis of what the institution can effectively absorb, assuming that there will be additional funding from the donors to cover the costs of the new unit's personnel and activities. It should, however, aim for a complement of three or four higher level professionals in Ouagadougou (a social scientist, an epidemiologist, a public health/management specialist, and a training specialist).

Broadening and Strengthening the EAC

50. We have proposed considerable additions to the responsibilities and structure of the OCP so that it can better address technical and institutional aspects of devolution and maximize it's potential impact on health systems development. We therefore propose, as well, that the JPC support an expanded EAC membership which reflects the growing importance of social and managerial issues to the future of onchocerciasis control in the region. Specifically, the committee should be strengthened by the addition of new members with extensive experience in public health management (especially chemotherapy delivery systems), training and institutional development, and the social sciences (especially with regard to community involvement in public health).

WHO/AFRO and Devolution

51. Because devolution is of necessity linked to general health systems development, there has been a demand for WHO/AFRO participation in planning for devolution. In collaboration with the OCP, WHO/AFRO recently prepared a planning document which discusses devolution in the wider context of health development strategy for the region (see WHO/AFRO/OCP 1989). This document is useful as a checklist of some prerequisites for successful devolution and it confirms the need for considerable external financing to begin setting these supporting structures and processes in place. The NOCs were not involved in the drafting of this document but it could be of value to each of the Participating Countries to guide their own review of country specific needs for devolution in the context of general health systems development. Although its potential financial contribution is limited, WHO/AFRO is encouraging the Participating Country governments to specifically earmark for devolution some

of the WHO/AFRO resources at their disposal. WHO/AFRO can thereby help to highlight the maintenance of onchocerciasis control as an important national health priority.

The Intercountry Facility

52. In the future, an intercountry facility will be necessary to support intercountry cooperation and maintain a regional perspective on onchocerciasis control. In particular, this facility will be needed to carry out essential activities that are not within the capability of any one of the Participating Countries acting alone.

53. In functional terms the intercountry facility should: (i) serve as a major information system to monitor onchocerciasis on a regular and regional basis in all of the Participating Countries in order to identify changing trends in the pattern of the disease and its recrudescence (it can make use of the extensive radio-network set in place by the OCP which has functioned very effectively); (ii) possess an active long-term memory against which to evaluate current action programs and each year it should generate a summary of surveillance results and steps taken for disease control; (iii) coordinate the efforts of different participants in a network of regional research institutions and disseminate information to the international community; and (v) undertake the training and technical assistance functions of the OCP Devolution Unit (as OCP eventually phases out its own activities).

54. In terms of structure, the existing options are few. In 1981, the Independent Commission indicated the OCP as the ideal base from which to develop an intercountry facility and some OCP professionals agree that a leaner OCP, with a new mandate, could do the job. Others have suggested that the OCCGE assume the role of intercountry facility, using the PAHO/WHO Caribbean Epidemiology Center as a model. At present, however, none of the United Nations organizations or intercountry technical cooperation agencies could be expected to provide the same quality and capability in onchocerciasis control as the OCP. One possible solution, therefore, may be to create an "onchocerciasis monitoring agency", to be operated by a small international team of disease control experts, which can combine the capabilities and coordinate the actions of existing regional research institutions and interested international agencies. The OCCGE Institutes, which are already used by OCP to train technicians and provide expert services, are possible candidates for such a network[5].

The Role of the Participating Countries in Devolution

55. On the whole, economies in the region are deteriorating and fiscal cutbacks have been especially damaging to health and social services. Efforts to reform health care in the spirit of Alma Ata, have not proven successful. There is a large gap between national governments and the needs of rural

[5] These include: the Institute of Tropical Ophthalmology in Bamako, the Pierre Richet Institute in Bouaké, National Institutes of Public Health in the Participating Countries, and several regional universities.

populations (Azarya and Chazan 1987; Decosas 1990) and health services have tended to have a low priority in the national budgets. Consequently, the Participating Countries have repeatedly called for external support of national health systems so that they can absorb and sustain the activities of devolution.

56. In this context, the potential fiscal contribution to devolution from the Participating Countries is clearly limited. Nonetheless, they can contribute significantly to the process of devolution. First, they can undertake the political task of making onchocerciasis a national priority. This is especially important in the core area where the success of the Program can work against it to the extent that onchocerciasis is no longer perceived as a problem. Public health authorities and the beneficiaries need to be firmly reminded that while the disease may be absent, the risk of recrudescence is not. Second, the Participating Countries must take steps to revitalize the NOCs. The need for this was a key conclusion of the 14th NOC meeting in Ouagadougou (May 1990). The NOCs should solicit assistance from the OCP Devolution Unit to help them identify issues and problems and to take steps to revitalize and strengthen their own efforts and participation in devolution. Third, members of the NOCs and other health ministry personnel can work with the OCP Devolution Unit to prepare the groundwork for health systems research and for later elaboration of human resource development plans. The Participating Countries can already begin to prepare inventories of what exists in terms of facilities, programs and human resources.

III. THE ONCHOCERCIASIS CHEMOTHERAPY PROJECT

57. The Onchocerciasis Chemotherapy Project (OCT) was constituted in 1983, following a recommendation by the WHO Independent Commission (WHO 1981) that a safe and effective macrofilaricide would contribute significantly to future strategic planning of OCP. It was recommended that the JPC provide the necessary resources from the Onchocerciasis Fund and delegate responsibility for the program to TDR. In December 1981, the JPC requested that WHO establish the OCT on behalf of OCP. When OCT was formally established in 1983, it was allocated a budget of US$3.45 million per annum for five years.

58. The stated objective of OCT is: to accelerate the discovery and development of a safe, effective, low-cost and easily administered drug for onchocerciasis, which will be suitable for large-scale use and which will meet the following criteria: (i) it must kill or permanently sterilize the adult female worms of Onchocerca volvulus, without at the same time causing severe allergic reactions in recipients from microfilaricidal action; and (ii) if it has a microfilaricidal action this should be of long duration, and reactions in the host should be minimal.

OCT's Major Activities

59. One of the OCT's most important activities has been collaboration with the pharmaceutical industry. OCT has supported two multidisciplinary research groups within drug companies (Welcome Research Laboratories and Ubjohn Co.) and has collaborated with three pharmaceutical companies on potential anti-Onchocerca compounds: Merck, Sharp, and Dohme (US), Janssen Pharmaceutica (Belgium), and Ciba-Geigy (Switzerland) (see Annex 4).

60. In collaboration with Merck, Sharp and Dohme, Phase I and II clinical trials of ivermectin were initiated against onchocerciasis. OCT also funded additional assays to explore potential problems of toxicity in laboratory infections of bacterial meningitis in dogs, and Trypanosoma rhodesiense infections in primates. Studies were also made of the possible prophylactic effect of ivermectin against developing larvae of Onchocerca volvulus in the chimpanzee (no such activity was apparent). In collaboration with Ciba-Geigy Ltd., two compounds, CGP 6140 and CGP 20376, which have macrofilaricidal activity against Onchocerca gibsoni in cattle, were introduced into Phase I clinical trials for onchocerciasis (CGP 6140) and lymphatic filariasis (CGP 20376) in 1985. In addition, OCT has collaborated with Janssen Pharmaceutica which has attempted to modify formulations of benzimidazole for either improved bioavailablity (mebendazole) or painless intramuscular injection (flubendazole) (neither of these objectives was achieved).

61. During the past two years, OCT has made a critical appraisal of all fundamental research projects, and only those essential to drug screening, or having potential for identification of drugs in the short term have been retained. Thus, the contracts with the Welcome Research Laboratories and the Upjohn Company consortium were terminated in June 1989, when leads showed toxicity and insufficient efficacy. Projects currently funded are directly related to drug screening, preclinical development and clinical trials.

62. The OCT has built up a network of in vivo screening facilities utilizing model filarial infections in rodents, and O. gibsoni and O. gutturosa in cattle. Laboratories were also encouraged to improve in vitro cultivation of Onchocerca species and other filariae to provide in vitro drug-screening facilities. As detailed in the Chemotherapy Project Progress Report in 1985 (WHO 1985), basic research was also carried out in various biochemical areas (see also WHO 1990a).

63. Furthermore, the OCT has funded the Onchocerciasis Chemotherapy Research Centre (OCRC) (originally located in Tamale, Ghana it is now in Hohoe), and has supported a mobile clinical research team, based in the United States which has conducted clinical trials in Liberia.

64. Since 1983, OCT has funded 73 projects, and the total cost of the program (to December 1989) is approximately US$15.9 million. Many scientific publications of high quality on basic biology and chemotherapy, funded by OCT, have been produced during this time (WHO 1990e). At present, OCT's most important contribution has been to assist in ivermectin development, in particular, in clinical trials. While not a macrofilaricide, this product has changed the prospects for short-term disease control, facilitated changes in on-going strategy, and has made feasible the planning and execution of devolution.

Earlier Reviews of OCT

65. In 1987, an Independent Review of OCT (WHO 1988a) drew several important conclusions and recommendations. It noted that the discovery of ivermectin as a long-acting microfilaricide had necessarily diverted a substantial proportion of OCT resources 1/. The review also noted that OCT had proven to be a good mechanism for promoting drug development in collaboration with industry and that a substantial scientific and financial investment was being made. Concluding that the general momentum gained should not be lost, the review recommended that, by 1991, alternative means of support be identified within TDR to ensure continuity in the long-term development of drugs against filarial infections.

66. In 1988, the CSA also undertook a review of the OCT to re-examine the OCT's mandate, management, and financing. Members of the donor community and the Expert Advisory Committee (EAC) participated in this review which reaffirmed that, with appropriate changes, the OCT would

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1/Ivermectin was registered as "Mectizan" for use against onchocerciasis in 1987, and subsequently, OCT handed over all other development of the drug at community level to OCP.

continue to provide the most satisfactory vehicle for support of macrofilaricide development and that the principal objective of OCT in future years should be the development of a safe and effective macrofilaricide consistent with feasible public health delivery. The review recommended that more pharmaceutical companies should be involved and that OCT procedures for drug discovery and development be changed to permit a more focused yet flexible management structure. It also recommended that more responsibility and authority (especially regarding collaboration with industry) be shifted from the OCT's Steering Committee to the OCT Secretariat. The review recommended that the function of the Steering Committee should be to evaluate scientific merit, progress and the level of funding of research contracts. It also recommended that US$7 million constitute the maximum in OCP support over the period 1989-1991, and that such support be fully integrated into the overall OCP budget.

67. The CSA review also recommended that future technical reviews of OCT be made by the EAC (rather than by TDR's technical advisory committee), and form part of the EAC's Annual Report to the JPC. It therefore recommended strengthening of the EAC in the area of drug development. In December 1989, JPC 10, on the recommendation of EAC 10, which favored further integration of OCT into the TDR structure, requested that OCP, Secretary OCT, and TDR, jointly prepare a scientific plan for macrofilaricide development for EAC 11 in 1990 (WHO 1989a).

68. Following the CSA review of OCT activities (WHO 1988a) it was decided to amalgamate the drug development resources of OCT with those of TDR for Filariasis (TDR/Fil), in order to improve the chances of success and reduce overall costs. The Preclinical Drug Development Team (PDDT) was therefore established which deals with matters of drug screening and development outside the usual Steering Committees. This has proven to be a very positive and valuable development.

The OCP/TDR Macrofil Project

69. At EAC 11 (1990), the Directors of OCP and TDR recommended that a joint OCP/TDR project be established for the development of a macrofilaricidal drug. The recommendation stated: "the activity must be focused on the search for a macrofilaricide, and not be diluted by other activities; that a streamlining gain must be achieved; and unnecessary changes be avoided". The proposal merges all macrofilaricide activities for both onchocerciasis and filariasis into one project management group. The OCP/TDR Macrofil Project is to be funded jointly by OCP and TDR, each making contributions that will be managed separately, i.e. there will be no change in present financial reporting of OCT resources, and TDR will establish a new budget line for OCP/TDR Macrofil. The OCP/TDR Macrofil Project will be, as in OCT, under the technical supervision of the Director of TDR. In order to avoid duplication of reports, a single report will be prepared annually which will go to the EAC and to TDR's technical advisory body (STAC). The Directors of OCP/TDR are satisfied that the arrangements outlined will facilitate any procedures necessary for the rapid development of a macrofilaricide, and at the same time provide accountability for the OCP/TDR Macrofil to both OCP and TDR. These arrangements were endorsed by EAC 11 in June 1990 (WHO 1990a).

Conclusions and Recommendations

70. Ivermectin was a serendipitous windfall from veterinary medicine which has now emerged as an acceptable microfilaricidal agent. The search for a macrofilaricide suitable for mass chemotherapy is, however, the prinicipal objective of OCT's endeavour and must continue to be addressed through screening of many more compounds from a larger range of pharmaceutical sources.

71. The urgency to find and develop a macrofilaricide may generate undue pressures on OCT, and it is understandable that every opportunity is taken, therefore, to screen compounds showing potential anti-onchocercal activity, particularly when preclinical work is undertaken by the pharmaceutical source. However, clinical trials of any compound, including GGI 18041 and CGP 6140 (see Annex 4) should not be pursued unless an acceptable toxicological profile is available.

72. Care should be taken that the goal of OCT to develop a macrofilaricide is not in any way diluted in the proposed future amalgamation of OCT with TDR Filariasis. Therefore, the status of the OCP/TDR Macrofil Project should be carefully monitored vis-a-vis future developments within TDR.

73. OCP/TDR should adopt a flexible financial policy with regard to special research and development costs which may arise in relation to a novel compound. In the event that a compound is found, the new OCP/TDR Macrofil Project should have the capacity to undertake the requisite preclinical and clinical trials. It may even be necessary to assist financially in research and development with respect to toxicological requirements such as carcinogenicity testing. Development costs of a novel compound will depend on parallel interests which the respective pharmaceutical source might have. It will, however, probably be necessary to provide extra budget to meet special screening needs.

74. OCT should continue to pursue development of a sensitivity assay for microfilariae of O. volvulus to ivermectin in order to detect possible resistance to the drug, especially in light of expanded population chemotherapy in the Western Extension and throughout the OCP area.

75. Industry should be made aware of known drug targets in filarial infections, and that drugs which may be produced for other purposes, particularly veterinary products, should be tested for antiparasitic activity in human infections. There is insufficient funding available to address basic research and rational chemotherapy development, without additional industrial input. Continued support for research on specific biochemical pathways is also important as well as efforts to identify new biological drug targets in filariae.

76. Representatives of the drug industry should be invited to participate in appropriate OCT meetings in order to encourage dialogue with industry.

IV. SOCIOECONOMIC DEVELOPMENT OF THE ONCHOCERCIASIS AREAS

Major Issues

77. The capacity for economic development of the onchocerciasis areas is limited in every country, therefore no country is now planning or implementing programs commensurate with the potential of the onchocerciasis areas.

78. In all eleven countries efficient allocation of investment resources cannot be undertaken outside the context of the national economy; independent planning for the onchocerciasis areas is probably inefficient and counterproductive. The Participating Countries should be encouraged to incorporate planning for onchocerciasis areas in overall country planning.

79. In all countries, fundamental requirements for effective economic development of the onchocerciasis zones are generally absent and need to be filled.

80. The question of adequacy of plans and actions can be approached with respect to the considerable efforts made by the CSA which inspired and assisted in onchocerciasis area studies undertaken by the Participating Countries, the "Hunting" report, the Land Settlement Review and the socioeconomic development consultations between each Participating Country and the CSA, led by the World Bank, as well as the comprehensive overall national development plans, actions, budgets and resources of the Participating Countries. Alternatively, the question may be approached with respect to the actual development plans and activities in the onchocerciasis zones, in the specific context of the overall national plans and development actions in each country.

81. Are the Participating Countries pursuing development opportunities in their onchocerciasis zones commensurate with the potential, relative to other investment options in the country in the context of the country's resources (including those available from external sources) and the social and political considerations confronting the decision-makers?

82. The answer to this queston is that the respective country authorities are undertaking the optimal choices in their circumstances. This response is, in a sense trivial, but in another, quite revealing: national planners and investment decision makers are aware of the potentials of their onchocerciasis areas and the priorities in the national schemes. National authorities may be overly informed, insofar as the OCP and CSA insist on focusing, perhaps too much, on onchocerciasis areas which may be relatively poor development choices in the national context. In other cases the onchocerciasis zones are the only alternative areas for development and in these instances the CSA/OCP efforts to steer development towards them may be irrelevant. Responsible investments are not undertaken just because certain sites are onchocerciasis-freed.

83. The OCP countries have often been overwhelmed by advice from donor international agencies and NGOs who insist on one or another development activity. This advice, which may come from the OCP as well, is based on objectives (motives) which may or may not be compatible with overall country goals.

84. Since the beginning of the Program, the CSA and the OCP have been preoccupied with development of the onchocerciasis zones. These efforts resulted first in a series of national impact studies (circa 1985) undertaken by the NOCs to identify (economic) effects and opportunities arising from successful control of onchocerciasis. These varied in quality but, in general, the results were poor. The CSA followed up with several major studies: The Hunting Report (Socioeconomic Development Studies in the OCP Areas), the Land Settlement Review and the National Oncho-Zone Development Studies. On the whole, these studies usefully contribute to a better understanding of the onchocerciasis zones as well as to relevant socio-demographic processes (e.g. land settlement). However, they should not be used to justify privileged development of the onchocerciasis areas. Rather, they ought to be incorporated into each country's overall national development plans in a realistic fashion.

85. At this point the Participating Countries have in hand a considerable amount of information about the onchocerciasis areas produced by themselves or by the CSA, as well as other studies, plans, and programs of national scope which are also of relevance to the onchocerciasis areas.

Assessment of potential productive activities

86. Both the Hunting studies and the World Bank-led CSA missions on socioeconomic development have addressed the question of development priorities in some detail. The Hunting studies generated a number of proposals and suggestions for National Oncho-Zone Development Studies and a priority development project for each of the seven original Participating Countries. The Bank's socioeconomic development missions reviewed these and further narrowed the choices. The Land Settlement Review provided useful insights and recommendations to additionally refine the possibilities. This External Review cannot in the time available do much to enhance what has already been done. We note however that it appears that the socioeconomic development program, proposed and carried out by the CSA since 1987, has accomplished just about all it can in attempting to promote economic development in the zone. Each of the preparatory studies and recommendations may well be justified in terms of its internal merits, but they can only be properly appraised in the national context and this has, generally, not been and probably cannot be done by the CSA/OCP or their various technical consultants. Development proposals in the onchocerciasis zone can only be properly addressed as a component of the country's overall investment planning. It is time for the Participating Countries to integrate the data, analyses and recommendations into their national planning and investment allocation processes.

87. We have attempted, in the country specific analyses in Annex 3, a subjective assessment of the possibility for significant development in the onchocerciasis zone given current economic conditions in each country, a sort of necessary "conditions precedent" for successful development in the zones, and the level of development activity underway or planned. Having done this, the interesting question becomes: Given the conditions of the respective national economies, the global priorities of the Participating Countries and the constraints confronting development of the onchocerciasis zones, what would be the most constructive activities for development of the zones at this time? While each economy has a different mix of constraints, there are some obstacles which are frequent and of possibly decisive importance. In order to expedite development in the onchocerciasis zone the Participating Countries should assure, as priorities, that: (a) agricultural price policy and marketing regulations must be consistent with free market principles, (b) land titling and transfers should be standardized and secure, (c) there is adequate physical access to areas appropriate for development and (d) the regulations and training necessary to assure environmental stability are in place. These will provide the minimal incentives to facilitate access and encourage individual initiative for sustainable development. Complementary priority inputs required in addition to these are: (a) adult literacy and relevant primary schools, (b) convenient water points for domestic use and (c) health care services.

88. Authorities in the Participating Countries must make their onchocerciasis zone decisions in the national socioeconomic development context. The best (and most efficient) contribution that the OCP can make to the economic development of the onchocerciasis zones is to continue its successful disease control efforts and to continue promoting general health services development through its involvement with local Ministries of Health.

V. CONCLUSIONS AND RECOMMENDATIONS

Protection of the Program's Achievements

89. In order to protect the OCP's achievements in the core area, the JPC must continue to support full-scale vector control operations in the extension areas, in particular, in areas which were sources of reinvasion of the original area. Operational research has confirmed that a minimum of 14 years of continuous larviciding is necessary to eliminate transmission of onchocerciasis. Therefore, larviciding should continue in these areas for at least that period of time. OCP can thus leave the Participating Countries in the best possible position to assume responsibility for maintaining onchocerciasis control.

Research To Define the Parameters of Ivermectin Use

90. The following research questions are essential to the future of onchocerciasis control. The JPC should consider the research needs identified here and adopt a list of research priorities. It must also consider and determine how these studies will be financed. Research is needed on: (i) the precise timing of intervention with ivermectin distribution to control recrudescence; (ii) the impact of ivermectin on transmission at more frequent dosages (e.g. 3 to 4 month intervals); (iii) the minimum safe interval between ivermectin treatments; (iv) the efficacy of ivermectin treatment over a prolonged period in preventing, halting or reversing eye disease; (v) the possible lesser impact of ivermectin in early infections and the implications for detecting and controlling recrudescence; (vi) all aspects of ivermectin delivery systems including behavioral/cultural aspects; (vii) development of an immunodiagnostic test to detect low levels of infection; and (viii) basic health systems research on the existing structures and capabilities in the Participating Countries in order to determine what will be needed to effectively implement ivermectin delivery and epidemiological surveillance. In addition, the Program should bear in mind the need for a future review of the epidemiological impact of ivermectin use in order to reassess its role in onchocerciasis control strategy.

Continue Support for Macrofilaricide Development

91. The OCP efforts, through the OCT, in drug development have been of great value. The field trials for ivermectin were instrumental in preparing for use of the drug in selective mass treatment to alleviate the symptoms of onchocerciasis. The need for a safe and effective macrofilaricide has not diminished, however. The new OCP/TDR Macrofil Project which will join OCT and TDR efforts in drug development for filariasis is a positive step which can enhance the search for a macrofilaricide. This effort should be fully supported so that an increased number of compounds from as many pharmaceutical sources as possible can be screened. OCP/TDR should adopt a flexible financial policy with regard to special research and development costs which

may arise in relation to a novel compound (e.g. toxicology testing). In addition, industry should be invited to participate in future Steering Committee meetings. Efforts should be made to increase industry awareness of known drug targets in filarial infections. Industry should be encouraged to test drugs produced for other purposes (e.g. veterinary products) for antiparasitic activity in human infections.

Maintain OCP's Successful Institutional Arrangements

92. The present institutional arrangements of the Program including each of its statutory decision making and advisory bodies should be maintained because they have been critical to the Program's success. The autonomy and flexibility of the Program, coupled with its checks and balances, have been essential in allowing it to plan effectively and implement efficiently while responding quickly to changing conditions and needs.

An OCP Devolution Unit

93. We recommend broadening the scope of OCP's functions through the creation of a Devolution Unit within OCP. This unit should employ at least 3 or 4 professionals (a social scientist, an epidemiologist, a public health/management specialist, and a training specialist) to: (i) assist the Participating Countries in preparation of human resource development plans; (ii) design and manage training and in-service training in multi-disease surveillance, drug distribution, and management; (iii) sensitize Participating Country governments to the need to establish onchocerciasis as a high priority in public health, to plan for the eventual absorption of OCP trained personnel in national structures and to promote relevant community education and mobilization activities; (iv) support operational research on topics relevant to devolution; and (v) provide technical assistance to Participating Country governments in order to strengthen organization and management of disease control.

An Intercountry Facility

94. The JPC must consider how to organize and finance the proposed inter-country facility which would function to: (i) coordinate onchocerciasis surveillance at a regional level; (ii) coordinate efforts of a network of regional research institutions involved in onchocerciasis research; and (iii) undertake the training and technical assistance functions of the OCP Devolution Unit when OCP eventually phases out its own activities.

Strengthening the Expert Advisory Committee

95. We also propose that the JPC support an expanded EAC membership which reflects the growing importance of social and managerial issues to the future of onchocerciaisis control in the region. Specifically, the committee should be strengthened by the addition of new members with extensive experience in public health management (especially chemotherapy delivery systems), training and institutional development, and the social sciences (especially in regard to community mobilization).

Socioeconomic Development

96. The CSA preparatory program on socioeconomic development, approved by JPC.7 in Accra in 1986, is nearing completion. We recommend that the CSA, interested donors and Participating Countries jointly support a review of what the CSA socioeconomic development program has produced. This review should be carried out by a team comprised of several economists and social scientists, working closely with Participating Country officials. Its primary objective should be to summarize the various conclusions of the socioeconomic development reports and then examine them in the specific socioeconomic development context of each of the Participating Countries. The team's country specific analyses and their interaction with country officials should help strengthen socioeconomic development planning with respect to the onchocerciaisis-freed areas and ensure the integration of such planning into the broader national development strategy of each of the Participating Countries.

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TERMS OF REFERENCE

ONCHOCERCIASIS CONTROL PROGRAMME
EXTERNAL REVIEW, 1990

I. Background

1. The Onchocerciasis Control Programme (OCP) is a multi-donor regional disease control effort set up in 1974 at the request of seven countries in the Volta River Basin: Benin, Burkina Faso, Ghana, Côte d'Ivoire, Mali, Niger and Togo. Four other countries joined the Programme in 1986: Guinea, Guinea-Bissau, Senegal and Sierra Leone. The OCP area presently covers about 1,300,000 km_2, with a population of 30 million. The Programme has been treating approximately 50,000 km of rivers throughout the OCP area.

2. The World Health Organization is the executing agency for OCP. Overall decisions regarding policy and planning for the Programme are made by a Joint Programme Committee (JPC) consisting of representatives of the 11 participating African countries, 23 donors and the four Sponsoring Agencies: the United Nations Development Programme (UNDP), the Food and Agriculture Organization (FAO), the World Bank, and the World Health Organization (WHO). The World Bank mobilizes funding for OCP, manages the Programme's trust fund, and is the principal contact with the participating donor community.

3. The Committee of Sponsoring Agencies (CSA), which is comprised of UNDP, FAO, World Bank, and WHO, acts as "steering committee" for the Programme. It meets quarterly to review work plans and budgets, monitor OCP operations, and examine reports prepared by the Programme's advisory bodies (described below). The CSA was assigned by the 1985 JPC the specific responsibility for coordinating preparatory socioeconomic development activities in collaboration with the 11 Participating Countries in areas where onchocerciasis control is underway. In response, the CSA has initiated a series of socioeconomic development studies to identify development opportunities and to propose follow-up actions in the onchocerciasis controlled areas of the Participating Countries.

4. The Programme is evaluated annually by an independent Expert Advisory Committee and an Ecological Group which provide guidance on scientific, technical and ecological matters. The members are experts in their fields who are selected by the Programme's Sponsoring Agencies.

5. In 1981 an Independent Commission reviewed the Onchocerciasis Control Programme and submitted to the Joint Programme Committee recommendations regarding the Programme's long-term prospects.

6. In 1985, the USAID undertook an evaluation mission on the Programme and prepared a report which was subsequently circulated to all members of the JPC endorsing the operational management and the success achieved by then.

7. At JPC.9 in Dakar a suggestion was made that "an external evaluation be conducted before the end of the Third Financial Phase to assess progress towards achieving Programme objectives and towards devolution and socioeconomic development."

8. In response, this paper draws up the Terms of Reference for an external review with a view to having a final report presented to JPC.11 in December 1990.

II. Objectives

9. The objectives of the external review are as follows:

(a) to take stock of OCP's progress to date, examine the reasons for OCP's achievements, and draw lessons which might have applicability to other projects and programmes;

(b) to assess progress towards devolving responsibilities to the Participating Countries for ensuring that there is no recrudescence of onchocerciasis, including strengthening national epidemiological surveillance and training capacities;

(c) to assess progress towards promoting future socioeconomic development of areas where onchocerciasis is now or soon will be under control; and

(d) to highlight relevant issues for the future of the Programme, to make appropriate recommendations for attaining OCP's objective, and to examine OCP's potential long-run contribution to health system development in the Participating Countries.

III. Terms of Reference

10. The external review should take into account prior conclusions and recommendations of the Expert Advisory Committee and the work of the CSA on socioeconomic development, as well as the findings of previous reviews and evaluations.

11. The external review team shall:

(a) take stock of OCP operations to date and the progress made in both the original area and extension areas in reducing the disease to a level where it is no longer of public health and socioeconomic importance;

(b) examine OCP's institutional arrangements and structure, including mechanisms for intercountry cooperation;

(c) assess the reasons for OCP's achievements and draw lessons which might have applicability to other projects and programmes;

(d) assess plans and mechanisms in place to distribute ivermectin, the effectiveness of the Programme's means for evaluating the epidemiological impact of ivermectin distribution, the cost of ivermectin treatment and its future budgetary implications, and the requirements for drug distribution mechanisms in the devolution phase;

(e) assess OCP and Participating Country activities currently underway or planned for strengthening the capacity of the Participating Countries to assume responsibilities for maintaining control of onchocerciasis;

(f) assess OCP's present and potential role in contributing to health care system development of the Participating Countries;

(g) assess the implications, both structural and financial, including an estimate of long-term recurrent costs, of maintaining control of onchocerciasis post-OCP, taking into account the difference in approaches required in the extension areas as opposed to the original area in view of the immediate active national involvement in OCP operations in the extension countries. This assessment would include studying the possibility of the need for some form of post-OCP institutional mechanism for coordinating control maintenance activities throughout the Programme area;

(h) review the progress and achievements of the Onchocerciasis Chemotherapy Project;

(i) assess the adequacy of the actions undertaken and planned to promote environmentally sound, sustainable socioeconomic development of the areas already, or soon to be, freed from onchocerciasis; and

(j) assess the potential of various possible productive activities within the onchocerciasis-controlled areas for future socioeconomic development.

IV. Coordination

12. The CSA will be responsible for organizing the external review team and assisting in coordinating its activities.

V. Composition of the Review Team

13. The CSA will select the external review team including the team leader. JPC members will be invited to propose candidates with relevant curriculum vitae for the team positions. The core team would consist of the following positions:

(a) Health Administrator. Must be qualified in public health administration with relevant experience in project and/or programme evaluation, as well as working on large health programmes and/or other multidisciplinary programmes in developing countries. Must be fluent in English or French and have a good working knowledge of the other.

(b) Tropical Disease Specialist. Must be qualified in public health and have experience in the epidemiology of tropical diseases and in the control of such diseases through large-scale control programs. Must have adequate experience in Africa. Must be fluent in English or French and have a good working knowledge of the other.

(c) Economist. Must be qualified general economist with relevant experience in project analysis, land/resource use, and rural development in developing countries. Must be fluent in English or French and have a good working knowledge of the other.

(d) Institutional Management Specialist. Must have experience with assessment of public institutions, and background in institutional management and international aid coordination, as well as knowledge of United Nations family of organizations and extensive experience in project/programme evaluation. Must be fluent in English or French and have a good working knowledge of the other.

(e) Executive Secretary. Must be qualified professional-level coordinator of activities, have familiarity with the United Nations system, and have had similar association with the planning and support of large-scale health programmes in developing countries. Must be fluent in English with a good working knowledge of French.

The team leader would be selected from one of the above candidates. He or she must be fluent in both English and French and must be accustomed to working with senior-level policy makers in African countries, United Nations agencies, and donor countries/agencies. In addition, the team leader would have the authority to recruit short-term highly specialized technical assistance, as required.

October 1989

COUNTRY DEVOLUTION PLANS: BURKINA FASO, MALI AND NIGER

Burkina Faso

1. Transmission of onchocerciasis has been interrupted in Burkina with the exception of a stretch of the Dienkoa river around the village of Pendie. The parasite reservoir has not yet been eliminated in the country but it is declining fast and is expected to become insignificant by the turn of the century. Larviciding may be interrupted at that point subject to the findings of extensive epidemiological surveillance. Burkina Faso's devolution plans provide for this surveillance in combination with detection of other diseases, trypanosomiasis, in particular. The plan also includes passive and active (mass) treatment with ivermectin.

2. Epidemiological surveillance will be carried out by mobile teams based in the provinces with the participation of fixed departmental health facilities and PHC posts served by volunteers (a male health worker, equipped with a bicycle, and a midwife). Distribution of ivermectin will be carried out vertically by the departmental level. The plan provides for mass treatment at least once a year and continuing passive treatment. It is anticipated that passive treatment will be problematic since beneficiaries would have to travel 10-15 kms to reach a distribution point. If this does not work the patient will also have to be reached vertically in villages which are not to be covered by mass treatment.

3. Under the present circumstances, this seems the most appropriate plan. As in other countries of the region, the integration of vertical and horizontal programmes will remain an ideal for the foreseeable future. Burkina, one of the poorest of the OCP countries, has established 5,704 PHC posts. Many do not operate and those which do are uncertain and problematic. Only half of the country's population is covered. Frequent abandonment of health posts may be due in part to the fact that staff are volunteers. The posts are insufficiently supervised and poorly equipped. Essential medicines are poorly supplied and stocks are often not replenished. There is a lack of accountability and communication with supervisory authorities. Community participation is insufficient or absent. The 57 medical centers operating at the departmental level under physicians are also poor in human and material resources. The same can be said of the Provincial Directorates of Health and Social Action. Generally the public health system, from the center to the village, has a weak structure and is poorly planned, administered and coordinated.

4. Devolution of OCP activities has been seen in Burkina (and in other countries in the same situation) as an opportunity for strengthening the national PHC system. In this case the devolution plan "falls within the frame-work of a policy of global development" (Burkina Faso 1988). The plan

was costed at about 600 million CFA in 1988 (roughly US$2.3 million) and is expected to be financed by external aid. Recurrent costs account for about 24% of the total. The cost of the plan is relatively low for a program that is so highly valued. However, plans are usually assessed not only with reference to their cost and value but also according to their potential effectiveness in the long term. In this respect Burkina has set a precedent which potential donors may hope to see in other countries. Devolution started in Burkina with external funding. The OCP, to promote devolution, contributed $CFA 5.0 million for the training of 195 nationals in epidemiological surveillance and drug distribution. Burkina has already established three out of six teams provided for in its devolution plan. Devolution will thus evolve in stages with formal evaluations proposed for each stage. The plan was to begin in 1989 but due to the lack of external funding it was postponed for two years.

5. The Ministers of Health and Planning have sought funding from several countries and international agencies but so far neither bilateral nor multilateral aid has been received. It seems that initially potential donors were not approached through the right channels and procedures and advice on these matters from OCP and international agencies did not come until recently. OCP has proposed that UNDP set up roundtable discussions with potential donors and UNDP has recently hired a consultant for this purpose. Generally, there has been a feeling of uncertainty about the intentions of donor countries and international agencies since the adoption of Burkina's plan. It now seems unlikely that the government will move ahead with devolution without external aid.

Mali

6. Mali's devolution plan covers the original area of OCP activities which represents about 40% of the country's territory and which has a high potential for socioeconomic development. Disease transmission is under control in this area with the exception of four districts where blackfly reinvasion occurred. The liberated zones have seen considerable economic development since the end of the drought. Significant immigration has followed and it is likely to increase. This, together with favorable climatic conditions and the termination of larviciding pose a serious threat of recrudescence of the disease (Mali 1989:9).

7. The whole of the original OCP area in Mali faces increasing prevalence of diseases such as trypanosomiasis and other blinding diseases. The control of these diseases will be combined with the activities to be devolved from the OCP.

8. Like Burkina, Mali has seen severe economic hardship over the past fifteen years. This is reflected in the country's poor demographic and health indicators. Only 25% of the population has access to health care (Mali 1989:11). Services are provided mainly at the district level and they are poorly financed, supplied, administered and staffed.

9. Mali's devolution plan proposes epidemiological surveys, active (mass) and passive treatment with ivermectin and monitoring of indicator villages every three years. Passive treatment with ivermectin is to be provided by district health centers which will be responsible for all activities concerning the control of onchocerciasis, trypanosomiasis and other blinding diseases. The proposed programme is a vertical one and basically satisfactory. It is to be evaluated in the third and fifth year of its operation. Its cost is relatively at the same level as that of Burkina's plan.

10. It must be noted that Mali's plan contains a Time-table of Activities which does not show any specific years. This is an indication of the country's reluctance to begin implementation of the plan before obtaining external aid. Attempts have been made to attract bilateral and multilateral funding but Mali has had no more success than Burkina in this respect. Progress towards devolution without such funding is doubtful.

Niger

11. Unlike the other countries of the original OCP area, Niger was not greatly affected by the disease when operations began. Only two regions, Say and Tera, along the Niger river were affected. The population exposed to the disease was 224,000 but only about 300 people were found to have impaired vision. Epidemiological surveys have shown that transmission of onchocerciasis is virtually interrupted in the whole area covered by the OCP. Although the reservoir of the disease has not been eliminated it is expected to decrease to insignificant levels after about fifteen years of control.

12. Niger is one of the poorest countries in the world and one of the first to establish a voluntary PHC network in the 1960's (about ten years before the Alma Ata Declaration). The country's devolution plan recorded this fact and declared that "Niger subscribes fully to the WHO's social goal, health for all by the year 2000" (Niger 1989:8). However, the country's vital statistics on the same page show a bleak picture which indicates that Niger is far from that goal.

13. The PHC system described in the plan is highly questionable. Information gathered during this review at the Ministry, and at the WHO representative's and in the field, indicates that the vast majority of the village health teams established in the country do not operate. About 80% of the population do not have access to care. Even in the relatively affluent region of Say about 15% of the village health posts have been abandoned. It is apparently for this reason that the country sees devolution of onchocerciasis control as a means for strengthening PHC (Niger 1989:13). A large part of the zone liberated from onchocerciasis, as many other parts of the country, have experienced environmental disasters due to erratic population movements and exploitation of resources. The government has planned a number of projects to address these issues but so far most of them remain on paper.

14. Niger's disease surveillance and treatment services have serious fiscal and administrative problems. The country relies heavily on external aid and/or "citizen participation" (privatization). The devolution plan presented by Niger has merit and combines onchocerciasis and leprosy control. It provides for vertical epidemiological surveillance and passive treatment with ivermectin at the local level. Surveillance is proposed only for permanent residents to be identified with the help of an interpreter, a highly problematic operation in areas with many nomads. Passive treatment is to be promoted by manuals and posters which are hardly appropriate means for rural populations. Although the plan declares that "special importance is attached to the management problems of public health services..." (Niger 1988:10) it does not make any provision for training in management (training and retraining is limited to technical staff).

15. The national budget includes no financing for the devolution plan. The Minister of Health applied to the UNDP for aid but the request was not processed since it is supposed to come from the Minister of Planning. This proceedure was only explained to the NOCs at the 1990 NOC meeting. Niger's devolution plan was to begin this year but, again, lack of external funding has delayed the process. As the area involved is relatively small, it is likely that the government will begin implementing the plan in order to attract external support.

SOCIOECONOMIC DEVELOPMENT: INDIVIDUAL COUNTRY PLANS

1. The situation in each of the eleven OCP countries differs in regard to the quality of data available, development progress to date, the kind and level of opportunities presented by the onchocerciasis zones, and the relative economic importance of these areas in the national context.

2. This report assesses the "adequacy" of development planning (formal or implicit) for the whole of the onchocerciasis zone in each country using several criteria which refer to the provision of basic conditions and inputs. These criteria are:(a) incentive agricultural price and marketing regulations; (b) secure land tenure; (c) road/track access; (d) domestic water supplies; (e) schools and health posts; and (f) environmental protection.

3. These criteria are particularly relevant to "new lands" exploitation; they apply especially to the portions of the onchocerciasis zone which are relatively underpopulated, but obviously not exclusively so. While fulfillment of these criteria alone would not be sufficient to attract agricultural development, we will assume that it is necessary. Therefore, adequacy of provision of the above inputs will be taken to indicate the "adequacy" of preparation for onchocerciasis zone development, regardless of the national economic context.

Benin

4. Benin appears to be taking some initial steps towards the transformation of a centralized economy into a more liberal and market-oriented one. The country does not have any unusual physical constraints to development. On the contrary, it possesses many advantages not enjoyed by its neighbors such as low population pressure, favorable climate, reliable rainfall, traditional food sufficiency, and a comfortable ratio of arable land per capita. It has had problems with mismanagement. Coming out of a bad economic situation, it is now, like many other developing countries, saddled with a huge external debt. There are other problems: The Ministry of Planning reported some 163 donor-funded projects currently (May 1990) at some stage of execution, in addition to those being planned or negotiated. Other observers report redundancy and waste or simply too much activity to the extent that "no one really knows what is going on." There is road construction but only limited maintenance, wells but no pump repairs, brush fires and limited land use planning. Internally, it is clearly in need of economic and regulatory reform. This will take time but already salutary effects are discernible.

5. With respect to the onchocerciasis zone (which here includes most of the country) development is integrated into the national plan. The Beninoise do not discuss "development of the onchocerciasis zone" *per se* (nor do the UNDP, FAO, or the World Bank). However, there is a great deal of ongoing rural development activity in Benin. Hundreds of kilometers of secondary roads, feeder roads and trails have been constructed or improved; hundreds of wells

and many dams have been built and market cooperatives organized; thousands of animal traction units are in use and more are being prepared. All this in the liberalization context which permits food exports through private commercial intermediaries, decontrol of some prices, (reduction or elimination of input subsidies) and efforts to improve rural incomes from food and export crop production. Overall, Benin appears to be well on the way to effectively exploiting the advantages provided by OCP (UNDP 1988).

Burkina Faso

6. As an original core country and the economy which has most to gain in economic terms (that is, proportionally, having had more land area affected by onchocerciasis than any other), Burkina Faso is both an example of the economic effects of the Onchocerciasis Control Program and, perhaps, the most crucial test of the ultimate utility of the Program. As elsewhere, onchocerciasis, when it was at its height, was not the only or even the most important factor underlying the elemental poverty which pervades the country; nor was it the most important constraint to growth and economic security. But the disease, in conjunction with the usual collection of other obstacles to economic improvement found in West Africa (in this case Sahelian W. Africa) was important. Moreover, the success so far of OCP in Burkina Faso, which has rendered essentially the whole country free from transmission of the disease, has occurred at a most opportune time.

7. Burkina Faso endured the droughts and after-effects of 1973-76 and 1983-84, the years of declining incomes, increasing population, emigration, environmental deterioration and political instability, economic deprivation, starvation and insecurity: the period which, more-or-less overlapped with the first decade of the OCP. It may be fortuitous coincidence that in Burkina Faso substantial economic improvement which began in about 1982, has continued into the present (1990) and appears to be continuing. In 1979, five years into OCP, the population was increasing, relatively modestly at about 2.3% but only due to substantial emigration, especially of productive young men. The major agricultural production area, the Mossi Plateau, was under increasing pressure from population, drought, reduced fallow, deforestation, and erosion. The better lands to the south, with higher rainfall, more permanent waterways, better forests and vegetation, and available underexploited arable land were not being employed (for a variety of reasons, one of which, of course, was onchocerciasis).

8. In comparison, in 1988 at least five hundred thousand additional hectares were under cultivation (60,000 ha. of which was reclaimed land); the area cultivated increasing at an average of 3% per annum. In the interval 1982-87 the area of irrigated surface doubled, increasing at an average of 2000 ha./annum, and these investments were mostly private sector initiatives. Exploitation of new lands increased in the south of the country, the area historically most affected by onchocerciasis. Interesting and encouraging events have been emerging in Burkina Faso, concurrent with the successful eradication of the disease.

9. There is no direct cause/effect link; although Burkina has, since 1974, been quite actively promoting development of its underutilized agricultural potential. The Volta Valley Authority (AVV) was given the responsibility for promotion of exploitation of the relatively sparsely populated and better-watered lands drained by the numerous permanent and seasonal rivers and streams in the south of the country. (At the same time substantial amounts of spontaneous, unassisted settlement was underway in the same broad area.) Much is being done, perhaps too much, in the sense that there are literally hundreds of projects under way, some 100 NGOs active in the country which tends to overwhelm official capacity to coordinate and efficiently allocate resources. This suggests that the donors need to explore the option of financing less and coordinating more their development support. In summary, however, the outlook for the economy, in part due to the success of OCP, is optimistic.

Ghana

10. Including the extension zone, the OCP covers some 2/3 of the surface of Ghana. Overall the zone is underpopulated and poor but has substantial agricultural potential. Since 1984 the government and its special National Onchocerciasis Secretariat, along with the FAO and UNDP, inter alia, have focused considerable effort on preparation for economic development of the zone. At this juncture, 1989, three observations might summarize the overall status: (a) There are not yet adequate data, analyses, understanding or identification of objectives (see Hunting 1988:146) to undertake investment in the zone; (b) The proposals which have emerged and the development measures even now underway are questionable; and (c) None of the studies or recommendations for the zone refers to the national context, the problems, resources, priorities and constraints to development of Ghana, as a whole. Nonetheless, the National Onchocerciasis Secretariat has prepared a "Planning Project" (SP 004/86) for the 1990-92 investment plan. This plan provides for road and bridge construction to access the "Overseas" areas from the north, health posts (partly to accommodate the devolution requirements for onchocerciasis) and water supply. (According to the National Onchocerciasis Secretariat, the roads portion has been funded.) The "Plan" does not address primary schools, land tenure (a chronic issue in the North) or environmental protection. This first phase pilot will cost some US$12 million and the outline for the long term envisioned by the National Onchocerciasis Secretariat would require an additional US$45-50 million over 12 years and is small in comparison with the recent annual national investment budgets (order-of-magnitude, US$200 million). While the National Onchocerciasis Secretariat identifies the zone as "the last remaining significant area in the Ghana/West Africa subregion which has not been exploited", it is not at all clear that the GOG itself believes this to be true and, if so, that national resources will be diverted accordingly.

11. Ghana is attempting to implement decentralization of development planning and operations. It has an established Northern Region development apparatus, nascent and flawed as it may be, and a number of special, donor-funded development institutions operating in the North which have defined

roles in the national development scheme. There is no obvious need for a separate National Onchocerciasis Secretariat. Ghana's planning for the onchocerciasis zone must be part and parcel of the national development process; it cannot be efficient otherwise because it is not being designed in the appropriate context.

Guinea

12. There was no way to go but up for Guinea in terms of national product and per capita income, since the country had declined to such a basic level by the mid 1980s when the Second Republic was organized. Very substantial improvements have already been achieved since reforms based upon a market orientation were begun in 1985. It appears that the necessary transformation will be pursued: the essential regulatory obstacles to agricultural production have been removed, producer prices are market-based, most subsidies eliminated such that food prices are not undercut by imports and farmers are free to make their own production decisions. Guinea has an endowment of human and natural resources that augur well for the future. Real and substantial growth has resumed; the problem is that there is so much to be done that the more remote rural areas, which comprise much of the onchocerciasis zone, are not likely to be given high priority.

13. The Government's development strategy is sensibly concentrating on global issues: research and extension, rural roads, water supply, encouragement of cooperatives and basic health and education. Resources are limited; the national accounts are oversubscribed; external debt overburdening and the civil service just emerging from decades of ineffectiveness. In the onchocerciasis zone there are many projects underway and many donors and NGOs in the field. In the circumstances discretion may be the optimal strategy: to assure that the private initiative of the farmers is given reasonable play (while attempting to assure sustainable systems of production) and to undertake to understand just what and where the development opportunities are i.e. (as suggested by the Hunting studies) to ascertain the land use patterns and identify their potential before committing substantial investment resources.

Guinea Bissau

14. Bissaun officials describe the present condition of the economy as transitional: from a very recent colonial experience and, more importantly, a protracted and extremely damaging war of independence. While most observers would agree to this, one must, in honesty also point out that the authorities adopted and attempted to implement a misconceived, centralist, directed economy. The country is undeveloped and, except for modest agricultural potential, resource-poor. Even today economic policy is guided by basic precepts such as: "setting of correct producer prices"; "proclamation that all land is property of the state"; "channeling rural surpluses to urban centers"; and "establishing uniform prices for the factors of production" -- precepts which are counterproductive and lead to inefficiency. Granted, the authorities nonetheless intend to "rededicate to family and private

agricultural production" and to reorganize and decentralize the Ministry of Agriculture and Rural Development. Under the reform program, rice import subsidies have been removed and domestic food price regulation has been largely eliminated.

15. The country is now well into its second four-year plan (the first having failed) and the second successive IMF/World Bank stabilization and restructuralization agreement. The National Development Plan in that section which addresses agricultural and rural development in the onchocerciasis zone (Region II, Bafata and Gabu plus a part of Oio) identifies the usual problems: access, markets, migration of young men, illiteracy, rudimentary technology and absence or inadequate supply of important inputs (seeds, improved fertilizer, implements, etc.) (Guinea Bissau 1988). As a result of liberalization of regulations agriculture has been growing rapidly recently. The dominant asset appears to be a substantial surplus of arable land, of which, particularly, the well-watered river valleys have promise. As part of the reorganization of the Ministry of Rural Development and Agriculture, the Ministry has identified the need for coordination of planning and execution of the many donor and NGO development activities in the region. Of the country's planned total investment in agriculture in the present plan, more than 50% is intended for the onchocerciasis zone. This would amount to the sum of approximately US$12 million for the four years of the plan. (In terms of per capita distribution, approximately, one-third of the total population lives in the zone.) These investments are intended for improved seeds, extension training, integrated rural development, cereal, honey and livestock production, access roads and irrigated rice (bas fond). Underlying this well-meaning and intense activity is a basic ignorance of resources and potentials, of actual land use and availability, of stream flows and water tables, topography and physical accessibility, demographics and population movements, commerce and markets (see Hunting 1988). This is acknowledged by the authorities who are promising to undertake the required surveys and censuses. (OCP has helped already in, e.g. monitoring streams and the carrying out of the base-line epidemiological census.) In the circumstances, there appears to be no way to intensify investment at this time; absorptive capacity is extremely limited relative to the many initiatives already underway.

Ivory Coast

16. The country has had, overall, relatively good growth (with serious setbacks, en route) into 1990. There are at this time major problems of external debt, debt service, high rate of growth of population and severe income disparities (modern versus developing sectors; urban and rural). Most of the growth and the wealth is in the south; the development problems and potential are in the center and north, the original core and extension zones of the OCP in the aggregate constituting two-thirds of the country. More than half the country is in the savanna zone, where the population growth has been minimal (as people have moved to the south). That portion of the country which was in the core area has the most sparse population density (excepting Ferkessedougou and Bouake) but it is endowed with some very attractive agricultural potential. In fact, presently it contributes a very substantial

proportion of the country's agricultural output: 1/3 of the rice, all of the sorghum and millet, all of the maize, 2/3 of the yams and the major portion of animal products. The Ivory Coast has done much already to improve output and incomes in the onchocerciasis zone; in addition, a considerable portion of the country's current investment program is channeled to the upper half of the country. The area of likely most rapid future agricultural growth is in the North (this has certainly been helped by the success of OCP) and it is here that the least developed, most "open" lands for settlement can be found. The considerable preparation of basic analyses already achieved by the CSA and with the time available now to complet other data requirements (e.g. maps and land use) the country will be in a better position to exploit the opportunities conferred by the success of OCP once macroeconomic stabilization and reform are achieved.

17. The Government does not single out the onchocerciasis zones for special planning but (quite properly) incorporates the zone into the country's national development planning process for which it has effective capability (see Hunting 1988).

Mali

18. The restructuring which was initiated in 1981 has definitely yielded benefits to the economy. Nonetheless, significant rationalization (i.e. liberalization) remains to be achieved. In the 1980's, the country was able to attain a modest positive real average per capita growth. That achievement vindicates the reforms that had been implemented and justifies continued perseverance and discipline on all fronts. Even in the best conceivable institutional and regulatory environment, the economy is constrained by its lack of physical resources, climatic vulnerability and the present technological capacity of the population.

19. Mali has correctly identified its principal resource potential in agriculture, but there are some aspects of the strategy and policy which are questionable. Although the authorities have made substantial progress in reform of agricultural policy, they continue to pursue inefficient goals (e.g. floor prices for basic food crops, regulation of markets and commercialization, and input subsidization). The policy of essentially subsidizing urban consumption at the expense of the cultivators continues to have a dampening effect on the output of basic foods. These, along with policies affecting land tenure and access to potentially productive areas have constrained development in the onchocerciasis zones.

20. Mali has undertaken decentralized planning (through the regional development committees) and implementation of development initiatives. (However, only about 5% of the national development program is channeled through the regional entities.) Much of the extension zone is considered unfit for cultivation; the core area in the Segou region is relatively more densely populated while having both poor aggregate cultivation potential and the shorter growing season. The Sikasso region portion of the core has

received a good deal of attention; it is the focus for development of cotton production (under the World Bank financed Mali Sud I & II & III projects) as well as livestock development, roads projects and numerous complementary activities. In the east of the onchocerciasis zone the potential for agriculture is relatively good (while the western half of the region has more moderate potential with mostly low suitability for cultivation). It is important to note that opinions differ on the availability of un or under-utilized arable lands. The Plan Quinquennal observes that level of exploitation in Sikasso Region is very high and dangerously close to overexploitation. Development plans for the region provide for construction and rehabilitation of major national north-south routes which traverse the area as-well-as a quantity of secondary roads and feeders. It is also important to observe that the Government of Mali does not, at this time, wish to encourage migration into the Sikasso region. (See Land Settlement Review, Mali Case Study) No provisions are being made for settlement into the core area.

Niger

21. The River Niger, which has ceased to flow at certain times in the recent past, is the only significant source of water in Niger and its banks are the best bet for cultivation in this desert and sub-desert country. Beyond mineral exports, agriculture (including livestock) serves as the base of the economy even though the agricultural potential in Niger is limited. Priority for development is given to enhancement of the river banks through irrigation development, etc. The only other possibility for cultivation is that small fraction of the country to the south and west of the river and the capital, Niamey. This area coincides, essentially with the onchocerciasis zone in Niger. It is not an especially attractive agricultural prospect. The land is generally open upland woodland with soils which are preponderantly classified as "marginal" or unsuitable for agriculture. Interspersed are alluvial valleys with seasonal streams and good potential. The region is attracting some spontaneous immigration. Immigration and natural growth increased the population from 60,000 in 1979 to 240,000 today. Onchocerciasis had been endemic in the area before OCP but at a low level; only about three hundred people were seriously affected. The limited soil fertility can reportedly be enhanced with additions of phosphates, some of which is available locally or nearby in Burkina Faso. The Government's plan for the area (Projet de mise en valeur des zones liberees de l'onchocercose), is comprehensive and includes ecological, agricultural, livestock, social services, education and infrastructure components. But there are many problems reflecting the distressed status of the national economy, making it difficult to invest public resources in this area in the short term. It seems likely, however, that the onchocerciasis zone will ultimately receive the investment attention which it merits. Niger has in the past demonstrated a capability for getting things done.

Senegal

22. The southeast quarter of the country, the Orientale, is in many senses the most remote and least appreciated section of the country; this (including a substantial portion of Bakel Province) is also the onchocerciasis zone. It is an area of endemic onchocerciasis. However, Senegal Orientale has not, historically, figured as an important region in the economy of Senegal and onchocercaisis has not been a major factor in its economic dynamics. While the operations of OCP have led to an effective national onchocerciasis team headquartered in Tambacounda, and this undoubtedly will yield improved rural public health services in the region, it is doubtful that the onchocerciasis control activities will have a significant impact on the economic development of the region.

23. The national economy of Senegal has been undergoing serious restructuralization since the crisis of the early 1980's. The country is still far from rationalization of its institutions and mastery of its finances. In the circumstances the country will necessarily concentrate on the principal problems and the long neglected Orientale region will continue to receive lesser attention. There is a regional development plan (1987) which incorporates activities of a number of donors and the cotton production parastatal, SODEFITEX, but it appears doubtful that the regional expectations will be met by the national plan. At the moment this policy of inattention to the Orientale may be appropriate. Although over the years there has been much discussion of need and a number of attempts to do something for the development of the East, it seems that there are not enough data in hand to decide what, if anything, should be done to initiate improvements (Hunting 1988:F327-329).

24. In Senegal, then, OCP operations have very little effect other than directly in public health and in the externalities resulting from the collaborative participation of the National Team. There is evidently little, if any, output from the National Onchocerciasis Committee and little evidence of consideration of the effects of onchocerciasis control in national or regional economic development. The GOS does appear, in principle, to be encouraging development of mining industry, but this is largely unrelated to onchocerciasis planning.

Sierra Leone

25. The Onchocerciasis zone has major agricultural potential, for rice and food crops. It is, on the whole, underpopulated, with promising stream valley sites uninhabited. The zone's population, which is, at most, only fifteen percent of the country total, has been growing modestly (less than 2%/annum) and has been receiving new settlers. There is a net out-migration, reportedly young males, and seasonal labor shortages have been cited (The Hunting studies) as a constraint to the success of some agricultural development.

26. Sierra Leone has much larger problems, and priorities, than the remote, North. The economic house has been out of order, not only in terms of external debt, arrearages, balance of payments and donor participation but with respect to issues basic to agricultural development and investment, such

as, food price policies and land titling, governmental administration and infrastructure. Real reform is just now being put on track. At this juncture, since development of (at least the upper) onchocerciasis zone is not all that pressing, certain activities necessary to prepare for future actions can be undertaken, such as, implementation of incentive regulations regarding agricultural production (price and marketing policies, land tenure) and basic studies of land use and planning (see the Hunting studies). There is as yet no development plan for the region.

Togo

27. The Onchocerciasis zone, including the extension, covers at least 90% of the country. Almost all development of agriculture in Togo, hence, all development planning is, effectively, planning for the onchocerciasis area. A fair assessment of the adequacy of the development effort in the onchocerciasis zone becomes an evaluation of Togo's overall development effort, which, perforce, must be addressed in the context of the country's access to resources i.e. its overall economic situation. Since 1983, Togo has been implementing stabilization and restructuring in cooperation with the IMF and the World Bank, in order to resolve excessive external debt obligations and to reform inefficient and counterproductive institutions and policies to optimal investment and exploitation of available resources. The effort has been paying off and some reforms are eliciting the desired responses.

28. In agriculture official measures to set prices for export commodities and food products have been eased. The Togolese government has abolished certain marketing monopolies, particularly for food crops (although the principle has not been abandoned). The result has been rapid growth in export and food production. (The Bank/Fund are urging cessation of taxation of export crops which have been an important source of official revenues.) The overall strategy for agriculture is to improve services including research, extension, input supply and improved seeds and to support the formation of cooperatives for credit, inputs, storage and marketing. Implementation of agricultural development initiatives, including projects, is through decentralized structures. Togo has significant unexploited agricultural potential and, overall, relatively mild population density (160 persons/sq. km of arable land) (World Bank 1988:37). Through the years agriculture has received much attention and donor investment. Currently there are literally hundreds of development projects in the rural areas, suggesting redundancy and inefficiency and overextension of official personnel and management capacities. Nonetheless, it seems that virtually all obstacles to agricultural development are somehow and somewhere being confronted; about 35% of the public investment program is earmarked for the sector. In summary, Togo's planning and priorities for development in the onchocerciasis zone are consistent with the problems, having removed a number of policy and institutional obstacles. A major near-term constraint may be degradation resulting from inadequate conservation measures arising from insecurity of land tenure.

THE ONCHOCERCIASIS CHEMOTHERAPY PROJECT (OCT)

Macrofilaricidal Development

1. CGI 18041. The benzothiazole derivative CGI 18041 is considered by OCT to be the most promising compounded from Ciba-Geigy at present. It is related chemically to both the earlier compounds CGP 6140 and CGP 20376. It is, however, more lipophilic, has different pharmacological properties to the other compounds, and does not produce the same high levels of the potentially toxic isothiocyanate metabolite. It has shown macrofilaricidal activity against Brugia malayi in the leaf monkey, using single oral doses of 25 or 50 mg/kg. It is intended that preclinical development work by Ciba-Geigy will be followed by Phase I clinical trails in man, provided that satisfactory preclinical toxicological data are available.

2. CGP 6140. This N-methyl piperazine adduct of amoscanate, was put into trials in Mali and Ghana. While interim reports from Ciba-Geigy relating to its own trials of CG 6140 in Latin America, indicate that multi-dose schedules of CGP 6140 (3mg/kg twice a day on three consecutive days) kill 70-75% of adult female worms, a slightly different dosage schedule in the clinical trials in Ghana and Mali resulted in neurotoxicity without macrofilaricidal activity (Dr. Awadzi, Hohoe, personal communication). Similar results were reported from Mali. The report of the Onchocerciasis Chemotherapy Project (WHO 1990d), however, stated that while the above mentioned dosing schedule, together with the low therapeutic ratio of the drug, make it unacceptable for routine community therapy, there is a possible role for the drug in combination with ivermectin in control of disease recrudescence in isolated foci within OCP. This is, indeed, an astonishing statement in view of the available toxicological evidence relating to the drug, and its low therapeutic index. Amoscanate and various formulations of nithiocyaminum have shown high efficacy in the treatment of schistosomiasis and macro- and microfilaricidal properties in appropriate test systems (Davis 1982). Side-effects of treatment, however, included central nervous system reactions and post-therapeutic jaundice of mixed cholestatic and hepatotoxic cause. While a substantial number of treatments for schistosomiasis were carried out in China, the drug has not been developed further for use in Western Medicine. It is, surprising, therefore, that clinical trials have been pursued using CGP 6140, even in light of the known unacceptable toxicology of amoscanate and related compounds.

3. CGP 20376. The compound CGP 20376, showed good macrofilaricidal activity in animal models of filariasis, but metabolism to an isothiocyanate metabolite produced problems of renal and hepatotoxicity. In clinical trials of patients infected with Wuchereria bancrofti, poor efficacy was found as a microfilaricide, together with reversible hepatotoxicity, and positive activity was detected in vitro tests for mutagenicity. The company and WHO therefore recently decided to terminate any further clinical trials with CGP 20376.

4. Suramin. Suramin, which is the only currently available macrofilaricide for individual patient therapy, has been used to treat a series of onchocerciasis patents at the Oncho Unit, Hohoe, Ghana. This was done using a standard multi-dose intravenous regimen of suramin. The condition of palpable nodules was monitored by ultrasound scanning, and these nodules will be removed at intervals throughout the period of a year for histopathological scrutiny. Blood and urine samples were taken for storage in the TDR/Fil Serum Bank, being tested for antigen and/or antibody changes. It is, therefore, hoped that such physical or immunological parameters may permit more precise estimates of worm damage, as a complement to the time-consuming histopathological technique. The eventual application of any such successful new methodology would certainly be a valuable adjunct in determining macrofilaricidal activity of new experimental compounds.

5. Other compounds. These have included benzimidazole and thiophanate analogues (University of Michigan, U.S.A.), supported by TDR/Fil. The results, however, are disappointing and it seems unlikely that any of the novel benzimidazole/thiophanates are superior macrofilaricides to the presently registered benzimidazole such as albendazole, mebendazole or flubendazole, which show only partical macrofilaricidal activity in man (WHO 1990d).

6. Other compounds continue to be selected and tested at Walter Reed Army Institute of Research (WRAIR), as are guanidine compounds from Parke-Davis, U.S.A.

Other Studies Supported by OCT

7. Additional studies necessary to the drug development process, and previously carried out within the industrial groups are now necessarily supported separately by OCT (WHO 1990d). Primary, secondary and tertiary screening in animals is supported in collaboration with the Justus-Liebig University Giessen, FRG, the CAB International Institute of Parasitology, St. Albans, U.K., the Institute for Medical Research, Kualar Lumpar, Malaysia, and the James Cook University, Queensland, Australia. Additionally in vitro drug assays are supported because of the lack of suitable animal models for Onchocerca infections. Such assays are carried out at the Institute of Parasitology, St. Albans, U.K. and at the Bernard Nocht Institute, Hamburg, FRG, with additional field work on O. volvulus being done in Ghana, Liberia and Guatemala.